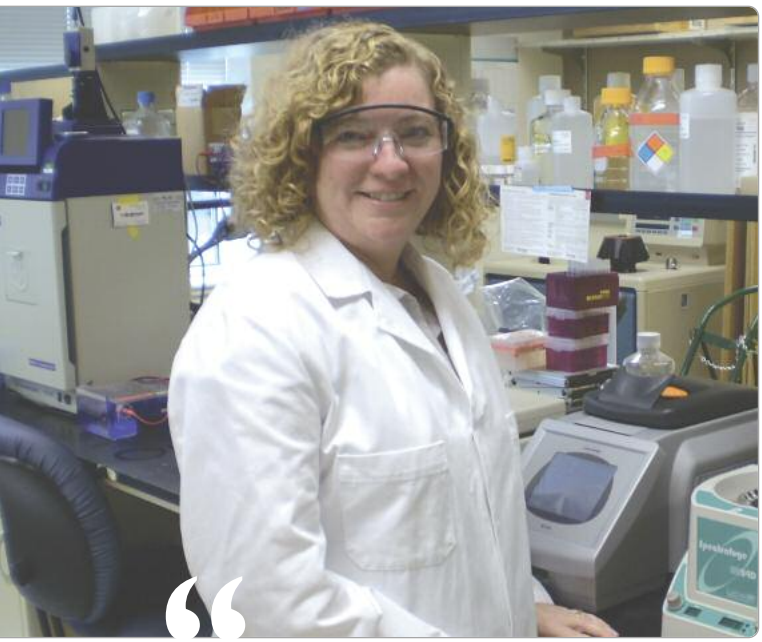
BY DENISE MYSHKO

PHASE II: Testing Efficacy, Planning for Marketing

New trial designs are helping pharmaceutical companies execute more efficient trials. This is also the time to begin thinking about the commercial aspect of a product candidate.



DR. NANCY BOMAN
Acucela

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Pharmaceutical companies and their partners are working to address productivity and create efficiency in Phase II development. New types of trial designs, such as adaptive trials, are being considered as solutions to these perennial issues.

"There are innovative ways in which biopharmaceutical companies are currently addressing the efficiency issue, which include population pharmacokinetic/pharmacodynamic modeling; conducting larger and potentially lengthier Phase I studies to exclude a suspected adverse event based on preclinical data before progressing to later stage development; and/or adaptive clinical trial design, such as a Phase IIb/Phase III run-in strategy," explains Howard Mayer, M.D., chief medical officer at EMD Serono. "In the latter scenario, multiple doses can be initiated in the Phase IIb portion of the program with the optimal dose selected based on prespecified statistical criteria and then continued into Phase III. We believe that taking the time to conduct more appropriate Phase I and Phase II trials can address these issues as early as possible in the drug development process, streamlining a complex, sophisticated process more effectively — resulting in a stronger, more efficient clinical trial approach."

Experts say adaptive designs allow the sponsor to make decisions earlier. This can result in fewer patients being required for drug-development programs. It could also result in shorter drug development timelines. Another benefit is spending less time on drugs that will never make it to the market.

"An adaptive trial design allows more targeted decisions to be made about further strategies for clinical development based on results to date, which can save time and money," says Nancy Boman, M.D., Ph.D., VP, clinical development and regulatory affairs, at Acucela. "Many companies are increasingly embracing adaptive trial designs and more flexible trials, which evolve based on the data they generated."

NATALIE DOUGLAS
Idis

In situations where the patient does not meet the trial criteria, an expanded access or named-patient program can provide well-regulated, well-controlled access to a new therapeutic option."

FAST FACT

REACTION TO MEGA-MERGERS, TIGHTENED R&D BUDGETS, AND MARKET ACCESS CHALLENGES LIE AHEAD FOR THE DRUG INDUSTRY IN 2010. IN FACT, THE DECADE WILL LOOK MUCH DIFFERENT FROM THE ONE JUST ENDED.

Source: Cutting Edge Information

Adaptive designs in Phase II trials define the right project plan and study design for maximum productive information in limited timelines, says Nagaraja Srivatsan, VP and head of life sciences, North America, at Cognizant.

"A Phase II and Phase III trial can also be seamlessly combined into one adaptive design, accelerating the clinical development process of the molecule," he says.

Adaptive designs are most beneficial in Phase II and Phase II/III trials because they allow sample size re-estimation, dose selection by adding or dropping treatment arms, and stopping the trial either for futility or extreme efficacy, says Martha Feller, Ph.D., global executive VP, operations, at i3 Research.

"Adaptive designs are used across most therapeutic areas, but most often in oncology trials," she says. "Adaptive designs also have potential benefit and utility in Phase III trials. But they have to be used with extreme caution and regulatory consultation to pre-

serve the integrity of the trial. In Phase III, they have been used to stop the trial for futility during the interim analysis if there is a big chance that the effect would not be demonstrated."

FDA officials say the agency is planning to publish a draft on adaptive designs sometime in March 2010, in time for a public meeting that FDA and DIA are sponsoring on March 26, 2010, to get public feedback.

Phase II: Preparing for Commercialization

By the time a compound reaches Phase II clinical development, companies need to start identifying, profiling, and developing pivotal relations with the appropriate leadership in the therapeutic area, says Mario Nacinovich, Jr., managing director, Axon Communications.

"It is at this stage that most companies empirically know if they are dealing with a mid-tier or niche product or if they have something truly revolutionary," he says. "The corresponding marketing spend at Phase II will focus on establishing important relationships. The company will need to make selections based on objective scientometric research, which encompasses bibliometric analysis, and traditional and more innovative social network analysis, and not on personal opinions or prior relationships."

Mr. Nacinovich says Phase II provides, in part, the foundation where equity originates and begins to be associated with the eventual brand.

"It is here that messages about the science and the early success of the brand are communicated in publications and early public relations activities," he says. "It is at this stage that some of the intangible concepts evolve and take hold as the foundation of eventual key assets of brand equity, brand identity, and brand vision. A critical consideration for the brand is how the investigators are engaged and educated at this early stage. This is an area that is often overlooked, but as competition increases and threatens the life cycle, companies need to invest in a more dynamic, interactive approach to investigator education."

Mr. Nacinovich says an advanced learning and motivational environment needs to be created to enhance knowledge and skill transfer at this stage and throughout the stages of the clinical trial process. There needs to be a focus on providing trial site and sponsor staff with the appropriate information and tools to ensure study objectives, for example patient and investigator recruitment targets and data quality standards, are achieved.

Laurie Lucas, founder and principal at L3 Healthcare Marketing, says marketing activities for precommercial products differ significantly from traditional brand and product marketing tactics.

"Precommercial marketing requires the collaboration of multiple brand stakeholders, including clinical affairs, preclinical, regulatory affairs, legal, medical affairs, marketing, and sales," she says. "Everyone involved with the brand should have an understanding of the broad commercial issues that will or are likely to affect the product when it reaches the market. The starting point is to develop an informed view of the market, which will help marketers identify hurdles and challenges, as well as potential solutions at an early stage. This process begins with extensive research into the market."

THE YEAR AHEAD

Experts from Cutting Edge Information predict there will be a continued tightening of R&D budgets in 2010.

Clinical groups are hard at work trimming timelines and expenses, even at a time when they're being pressured to be more productive. Average per-patient costs have leveled off, according to longitudinal studies, which is one positive sign.

While the CRO industry is expected to continue its growth, especially in new markets and in China, market access departments may experience some adjustments because of healthcare reform efforts, with the biggest impact coming on the payer side.

Additionally, the EDC vendor landscape is changing as part of the larger trends in the e-clinical ecosystem. With product offerings increasingly bundled and growth in both hosted and software-as-a-service offerings, the market is opening up to smaller life-sciences companies, enabling these companies to consider conducting and managing their trials directly.

Source: Cutting Edge Information.
For more information, visit cuttingedgeinfo.com.

LAURIE LUCAS ■
L3 Healthcare Marketing

"Marketing activities for precommercial products differ significantly from traditional brand and product marketing tactics."

NAGARAJA SRIVATSAN ■
Cognizant

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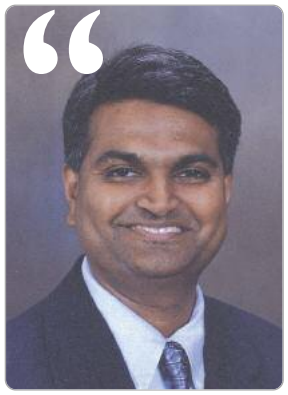

DR. MARTHA FELLER ■
i3 Research

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A few areas to understand include current treatment approaches, new treatments on the horizon, potential reimbursement scenarios and hurdles, patient population segmentation and identification.

"Analysis and assessment of this information will uncover key drivers and potential hurdles," she says.

The last critical step, Ms. Lucas adds, is to integrate these key learnings into strategic plans such as clinical development, regulatory, marketing, and managed markets.

"Ultimately, this knowledge will enable and empower the product development process, guide and inform critical decision-making processes, and greatly enhance the future success of the product," she says.

Industry leaders say this is the time to reach out to key opinion leaders. Dr. Boman says KOLs can provide state-of-the-art insights into realized and possible imminent clinical challenges encountered during the study conduct.

"By actively participating in advisory board discussions about trial design, they can help with planning and avoid potential pitfalls," she says. "KOLs can play an important role by identifying new investigators and promoting recruitment. Based on their experiences, they can also provide information on cutting-edge technologies and measurement methodologies to refine clinical trial design and data collection."

MARIO NACINOVICH JR. ■
Axon

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Mr. Srivatsan says KOLs provide guidance on structuring clinical trial protocols to generate credible, convincing, and differentiated data in line with the therapeutic needs that can be best addressed by an investigational product.

"These thought leaders can identify any safety concerns or issues with study design at the early stages," he says. "They can identify recruitment challenges and issues with inclusion/exclusion criteria; provide guidance to correct the site profile for the required patient pool; and provide guidance on current standard treatment practices and acceptable levels of study treatment.

"KOLs can also provide opinions on target product profiles, analyze the current competitive products, and uncover unmet market needs," Mr. Srivatsan adds. "They can also offer considerations for product labeling, all of which are helpful to build up Phase II and III developmental strategies for the compound."

Most people would agree that the primary audience at this point is the physician, says Robert Norris, founder and president of Complete Healthcare Communications.

"But at the end of the day, because patients are such strong advocates of their own disease states, we'd be foolish not to be aware they are becoming an increasingly strong part of the audience that we need to address," he says. "I don't think it's uncommon for a patient to visit a doctor with an article and say, can you tell me what's going on with this study? And the doctor may not have known about it. So, as patients become more and more their own advocates — specialists, really, in their specific disease state — they become a necessary part of the communications picture. They may still not be the primary focus, but they are definitely a presence."

Clinical trials are not the only way a patient can gain access to an investigational drug. Since the 1970s, FDA-sanctioned expanded access programs have enabled patients, under specific circumstances, to access drugs or biologics that are still in development.

"The FDA recently updated its expanded access regulations to ensure broad and equitable access to investigational drugs for treatment purposes," says Natalie Douglas, CEO of Idis. "For patients who are terminally or seriously ill, who have exhausted all available therapies, or who cannot enter a clinical trial, access to an investigational drug or biologic outside the trial setting can represent a new treatment option."

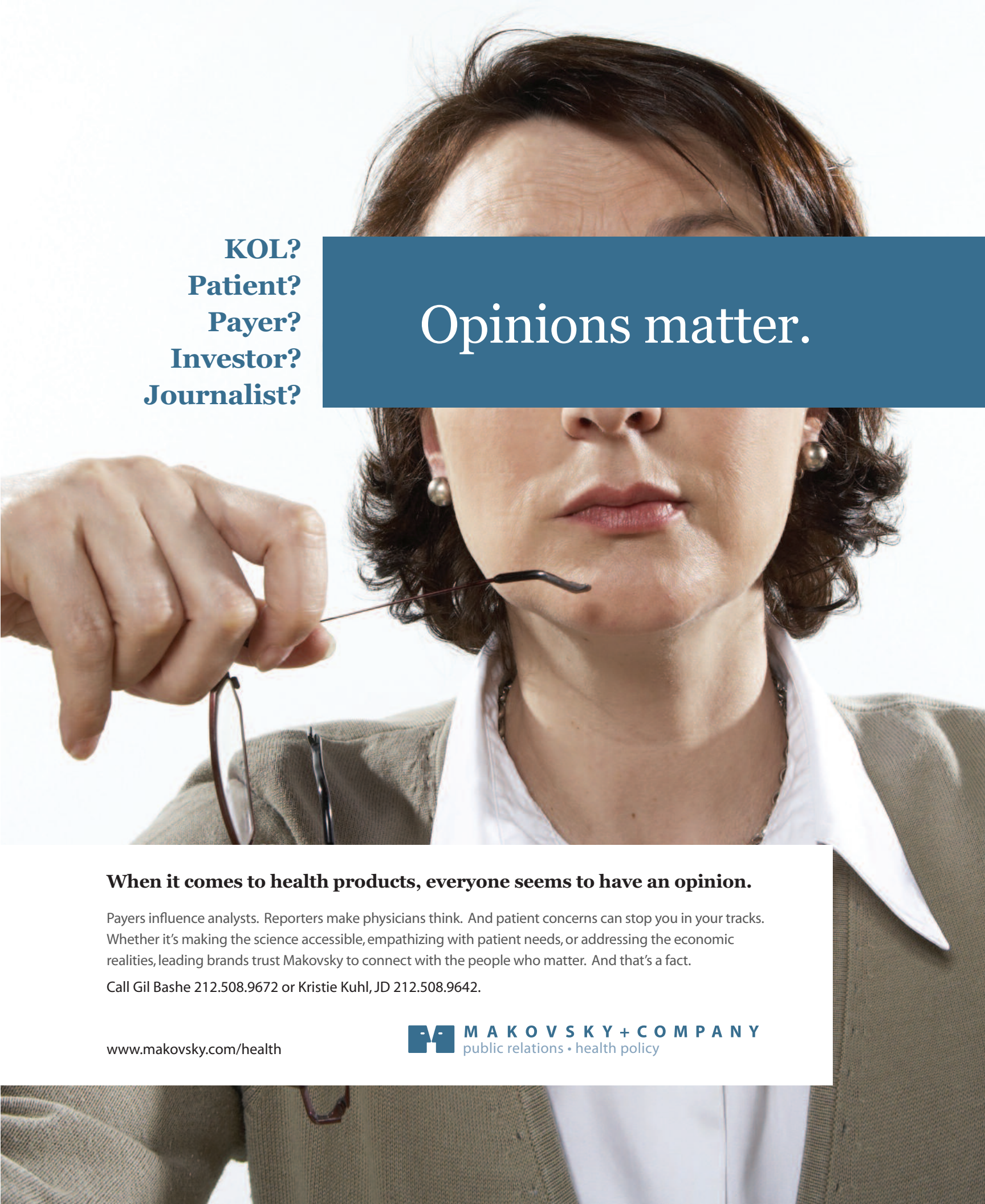
In addition to the recently updated FDA regulations, the trend toward greater transparency of drug development pipelines and the accessibly of powerful social media tools have led to a more informed, empowered, and vocal population of patients around the world.

"As a result, the focus on expanded access is likely to intensify and result in an increased number of requests for access to drugs before approval or launch," she says. "Companies should be prepared for these requests."

Ultimately, the choice to offer expanded access — or not — is left up to the developer, says Hal Barron, global head, product development and chief medical officer, at Roche.

"FDA regulations do not force companies to offer access to their investigational drugs," Mr. Barron says. "When considering this option, however, companies must undertake a thorough evaluation of important questions such as when to offer access and for which patients." ✦

PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.



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